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Attorney Docket No. 3229/1/PCT

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

IN RE APPLICATION OF:	)	
	)	
GARY S. JACOB	)	
and	)	EXAMINER:
RAYMOND A. DWEK	)	
	)	
SERIAL NUMBER: 10/031,767	)	
	)	
FILED: JAN. 23, 2002	)	GROUP ART UNIT:
	)	
TITLE: COMBINATION DRUG	)	
THERAPY FOR GLYCOLIPID	)	
STORAGE DISEASES	)	
	)	
Corres. to:	)	
PCT/US00/16340	)	

**RESPONSE TO NOTIFICATION OF MISSING REQUIREMENTS UNDER 35 U.S.C. 371  
IN THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US)**

Commissioner for Patents  
BOX PCT  
United States Patent and Trademark Office  
Washington, D.C. 20231

Dear Sir:

This is in response to the "Notification of Missing Requirements Under 35 U.S.C. 371 in the United States Designated/Elected Office (DO/EO/US)" mailed 04/08/2002. A copy of said Notification identified as "Form PCT/DO/EO905 (371 Formalities Notice)" is enclosed herewith as required.

**REMARKS**

According to said Notification, it is stated that:

- The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 CFR 1.821-1.825.

Further according to said Notification, applicant is required to provide:

- An initial or substitute computer readable form (CRF) of the "Sequence Listing"
- A statement that the contents of the paper or compact disc and the computer readable form are the same and, where applicable, include no new matter...

In response to said Notification, it is respectfully submitted that:

SAID NOTIFICATION IS IN ERROR SINCE THIS APPLICATION  
DOES NOT CONTAIN ANY NUCLEOTIDE OR AMINO ACID SEQUENCE.

- I. The present application was filed without a Sequence Listing because the disclosure does not contain any nucleotide or amino acid sequences. Therefore, the Sequence Rules 37 CFR 1.821-1.825 do not apply to this application.
- II. The chemical compounds disclosed in this application are carbohydrate compounds and/or organic molecules that do not contain any nucleotide or amino acid sequences.
- III. The disclosed carbohydrate compounds and/or organic molecules are, e.g.,
  - Cyclic organic ring compounds such as N-butyldeoxynojirimycin (abbreviated NB-DNJ) and analogs thereof. As is well known, these compounds have an imide ring with only one nitrogen in the structure and several hydroxyl and alkyl groups. The deoxynojirimycin (DNJ) portion of the molecule is a carbohydrate that has alkyl groups attached to the ring nitrogen. Enclosed herewith for the information of the Office is a copy of abstract number 2887 from *The Merck Index*, Eleventh Edition, 1989, which shows the carbohydrate chemical structure of deoxynojirimycin.

Glycolytic enzymes such as glucocerebrosidase,  $\alpha$ -glucosidase, and ceramide glucosyltransferase, and their glycolipid substrates, e.g. glucosylceramide (abbreviated Glc-Cer in Fig. 1) and lactosylceramide (abbreviated Lac-Cer in Fig. 1). These substances have glycolytic carbohydrate structures rather than nucleotide or amino acid sequences. Thus, ceramide is the hydrophobic portion of a glycosphingolipid. See, e.g. the sphingolipid structures shown in the attached copy of the article by Sweeley et al., "Structure and Metabolism of Glycolipids", p. 48, in Walborg, *Glycoproteins and Glycolipids in Disease Processes*, ACS Symposium Series 80, 1978. It should be noted that there is only one nitrogen in these structures which, therefore, cannot constitute any nucleotide or amino acid sequence within the Sequence Rules.

- IV. It is believed that said Notification is based on a misunderstanding of the chemical structure of the carbohydrate and organic molecules disclosed in the present application.

Perhaps it was erroneously concluded by the PTO that the structures shown in FIG. 4A, 4B and 4C are nucleotides and/or peptides. Instead, as stated at page 10 of the disclosure:

FIG. 4A is a representation of the structure of the glucosylceramide. As is well known, ceramide is an N-acyl fatty acid derivative of sphingosine. Enclosed herewith for the information of the Office is a copy of abstract number 8703 of The Merck Index, which shows the organic chemical structure of sphingosine, and a copy of abstract number 2800, which shows that ceramide is a N-acyl fatty acid derivative of sphingosine. It should be noted that there is only one nitrogen in the structure.

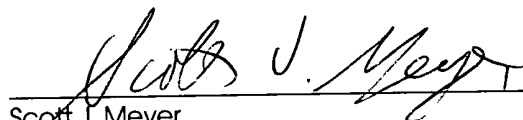
FIG. 4B is a representation of N-butyl deoxynojirimycin (DNJ), already discussed and illustrated above in part III.

FIG. 4C is an overlay of the ceramide structure of 4A and the NB-DNJ structure of 4B.

- V. Applicant also calls attention to the fact that after the filing of the PCT application PCT/US00/16340, the International Search Report was mailed 22/11/2000 and the International Preliminary Examination Report was mailed 05/04/2001. Said Reports were correctly made without there being basis to any nucleotide or amino acid sequence disclosed in the application. If there were any nucleotide or amino acid sequence disclosed in the application, surely the International Preliminary Examining authority would have acted thereon.

In view of the foregoing remarks and enclosures, it is respectfully submitted that the Notification of Missing Requirements Under 35 U.S.C. 371 be withdrawn and that the application be processed for examination.

Respectfully submitted,



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Attorney for Applicant

SJM/mr

May 14, 2002

Enc. Abstracts 2800, 2887 and 8703 from *The Merck Index*  
Walborg, *Glycoproteins and Glycolipids in Disease Processes*, p. 48  
Form PCT/DO/EO905 (371 Formalities Notice)